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PRESENT STATUS OF PROBLEMS OF BLOOD SUBSTITUTES,
THERAPY OF BURNS, AND RADIATION SICKNESS

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The 34th Plenary Session of the Scientific Council of the Central Order of Lenin Institute of Hematology and Blood Transfusion (TsOLIPK), which took place on 23-28 May 1955, summarized the results of work on problems involving the use of blood substitutes and connected with the therapy of burns and of radiation sickness. Representatives of the widespread network of the blood transfusion service, the chief surgeons of the ministries of union republics, members of kray and oblast health departments, and representatives of a number of scientific research and therapeutic institutions took part in the work of the plenary session.

At five meetings devoted to the problem of blood substitutes, the classification and evaluation of available blood substitutes, together with the mechanism of their action and their therapeutic effectiveness, were discussed.

In the program report given by Prof. A. A. Bagdasarov, Corresponding Member of the Academy of Medical Sciences USSR, the contemporary state of the problem of blood substitutes and the prospects of further developments in this field were outlined.

According to Bagdasarov, the blood substitutes which are available at present can be subdivided into three basic groups: blood substitutes derived from isogenic blood (plasma and serum); blood substitutes which contain intact protein molecules obtained from heterogenous blood (LSB, EK-8, and Colloidal Infusin TsIPK), as well as preparations related to them, such as protein hydrolysates representing products of the splitting of proteins (hydrolysate L-103, protein hydrolysate TsOLIPK, and amino-peptide); synthetic blood substitutes (substances of the type of dextran and periston).

Effective blood substitutes must first of all eliminate hemodynamic disturbances, i. e., raise and persistently keep at the necessary level the blood pressure, preserve the volume of circulating blood, and assure parenteral nutrition of the organism.

In a report by Prof. A. N. Filatov, Corresponding Member Academy of Medical Sciences USSR, an evaluation of currently available blood substitutes was given and the conditions with which blood substitutes must comply as far as their development and testing are concerned were discussed.

In reports by Prof. D. A. Arapov (Moscow), Corresponding Member of Medical Sciences USSR, Prof. N. N. Milostanov and his collaborators (Khar'kov), Prof. N. I. Blinov (Leningrad), Prof. T. A. Nalivkin (Odessa), A. A. Chernyavskiy, and A. F. Cheremukhin (Gor'kiy), clinical data were cited which have a bearing on the investigation of the action of blood substitutes derived from heterogenous blood. These data indicated that such blood substitutes have a considerable therapeutic effectiveness. For instance, Prof. Milostanov reported on the favorable effects obtained by him and his collaborators in the use of Belen'kiy's therapeutic serum (LSB) and of EK-8 in cases of traumatic and surgical shock, in various diseases accompanied by disturbances of the hemodynamics and in toxicoinfectious conditions accompanied by hypoproteinaemia (burns, peritonitis, intestinal obstruction, etc.). A number of serological investigations have established that the therapeutic serum possesses antigenic properties (precipitinogen is present in it) and that it produces antibodies in the organism of recipients.

STAT

Prof D. A. Arapov, Corresponding Member of the Academy of Medical Sciences USSR, summarized his own observations and data obtained from various therapeutic institutions on the results of the clinical application of LSB. Arapov is of the opinion that notwithstanding the rather strong tendency of this preparation to produce reactions, it has proved to be a very good liquid blood substitute and agent for the parenteral feeding of patients.

V. A. Agranenko and M. I. Nikolayeva pointed out the therapeutic effectiveness of LSB in operations carried out on organs of the thorax and of the abdomen. They stated that this serum has a favorable effect on the vascular tonus and that it normalizes disturbances of hemodynamics, so that the application of whole blood could be curtailed in operations carried out in cavities with its aid. In the opinion of these investigators, it is advisable to combine a transfusion of LSB with a transfusion of blood whenever there are considerable blood losses and also whenever major operations are carried out on the organs of the thorax.

However, although LSB has many positive qualities, experimental and clinical observations have confirmed that it exerts anaphylactogenic effects with the result that post-transfusion reactions and complications of the anaphylactic type are often encountered after its use.

Clinical observations carried out by workers at the Central Institute of Hematology and Blood Transfusion (L. N. Pushkar' and A. I. Tarakanov) on the application of LSB established that the reaction of patients to intravenous introduction of LSB, which arises because of the anaphylactogenic properties of this serum, depends to a considerable extent on the initial condition of the recipient, the nature of the pathological process, the number of transfusions which have been carried out, the time which has elapsed between the transfusions, and the method of administration of the preparation. To prevent the occurrence of reactions and complications, these investigators consider it advisable to use the drop method for the administration of LSB. They recommend that the first five milliliters be not administered at a rate greater than 30 drops per minute. Particular care must be taken in administering this serum to patients who have a heightened reactivity because of allergic conditions, Basedow's disease, or gastrointestinal ulcers.

Clinical investigations by Pushkar' and Tarakanov have shown that application of anesthetics such as novocain, morphine, and dimedrol in connection with the transfusion of LSB does not exert a noticeable effect as far as reduction of the incidence of reactions and of the occurrence of these reactions is concerned.

The frequency of the incidence of reactions and complications following transfusion of LSB is not uniform on the basis of a comparison of data communicated by different authors. This can be explained by differences in the time elapsed between transfusions of LSB and the use of different indications for transfusions.

M. L. Garfunkel' and L. A. Danilova (TsOLIPK) reported on the results of an investigation of functional and morphological changes in animals upon introduction of heterogenous blood substitutes (LSB). Pathological investigations of the organs of animals killed at different times have shown that a single administration of LSB brings about disturbances of blood circulation and lymph circulation which are expressed to a different degree. Some dogs develop necrotic changes in the liver and kidneys and a reaction in the tissues surrounding these organs.

STAT

G. P. Vinokurova, I. I. Zaretskiy, and I. A. Mikhaylova demonstrated that changes in the functioning of the kidneys which proceed in two phases take place after the transfusion of citrate blood. When the blood which is being transfused has been kept for a longer period of time, the hemotransfusion produces more sharply expressed functional changes in the kidneys of the recipient. The changes in the functioning of the kidneys after transfusion of LSR proved to be still more pronounced.

Reports by Prof Yu. A. Spasokukotskiy, Z. L. Chernogorova, I. P. Sarnitskiy (Kiev), A. A. Chernyavskiy and L. F. Cheremukhina (Gor'kiy) and A. P. Kachov (Moscow) dealt with investigations of the new heteroprotein blood substitute BK-3. Many-sided and numerous investigations by these workers have shown that BK-3 is effective as far as its hemodynamic, antishock and therapeutic action is concerned. As compared with LSR, the anaphylactogenic properties of BK-3 are less pronounced. However, the clinical investigation of some plant batches of BK-3 has shown that this preparation has toxic properties. This toxicity is apparently connected with shortcomings in carrying out the process for the production of this preparation.

Great interest was elicited by the new heteroprotein blood substitutes which were discussed at the session, i.e., parenterin (Prof N. G. Belin'kiy and collaborators), L-102 (Prof L. G. Bogomolova), and the serum proteins TsOLIPK No 1 and 2.

Prof P. S. Vasil'yev, N. A. Aleksandrovskiy and collaborators, Prof N. A. Fedorov, V. V. L'vova, and P. I. Pokrovskiy reported on detailed investigations dealing with the new protein hydrolysate TsOLIPK, which represents a highly effective agent for the parenteral nutrition of the organism. When an appropriate technique of production is applied, one succeeds in obtaining hydrolysates which are completely devoid of anaphylactogenic properties and do not produce any reactions. The amino acids which are contained in the protein hydrolysates are included into the nitrogen metabolism and are assimilated by the organism, so that the requirements of the organism for proteins in the absence of normal nutrition through the gastrointestinal tract are satisfied. Of the same type as the TsOLIPK protein hydrolysate is the preparation L-103 proposed by the Leningrad Institute of Blood Transfusion and also the aminopeptide which has been developed at the Military Medical Order of Lenin Academy imeni S. M. Kirov by Professor Kalmykov. These preparations are very promising as far as applications in connection with practical surgery are concerned because they adequately solve the problem of parenteral nutrition.

Z. A. Chaplygina (Leningrad) reported that it is possible to use coagulated isogenic blood which remains after the preparation of serum and of erythrocytic mass for the production of an isogenic preparation named aminokrovin.

G. Ya. Rozenberg, K. M. Dvolaytskaya — Baryshova, and collaborators presented experimental data on the biological synthesis and chemical characteristics of a preparation of the dextran-poliglyukin [sic] type.

In reports by V. A. Agranenko and R. I. Muranyan, clinical data were presented which indicate that poliglyukin has a considerable therapeutic effectiveness when used in the treatment of traumatic shock and the consequences of acute losses of blood.

STAT

Prof M. D. Shestakovskiy, Prof P. S. Vasil'yev, and collaborators reported on the great importance from the therapeutic standpoint of the synthetic blood substitute polyvinylpyrrolidone (periston). They have developed a method for the production of polyvinylpyrrolidone and have studied its properties. V. B. Koziner (TsOLIPK) presented experimental data on the effectiveness from the hemodynamic standpoint of colloidal solution of polyvinylpyrrolidone when used in the therapy of the consequences of acute blood losses.

In a report by G. V. Sukyasyan (TsOLIPK), experimental data were given on the comparative therapeutic effectiveness of different antishock liquids. The author of this report is of the opinion that the most effective preparations in the treatment of traumatic shock are antishock liquids prepared according to Prof E. A. Asratyan and Prof N. A. Fedorov. The reports on blood substitutes that had been heard resulted in a discussion. It was noted during the discussion that at present the best blood substitutes are still isogenic plasma and isogenic serum. However, the limited facilities for producing them in large quantities lead to the necessity of using heteroprotein substitutes. Further research on the development of a good species nonspecific serum which does not produce any reactions is necessary. Particular attention must be paid to protein hydrolysates and synthetic preparations, which should be used depending on the type of the pathological condition. Hydrolysates enable one to administer protein nutrition extraintestinally, while the synthetic blood substitutes have a high capacity to restore disturbances of the hemodynamics.

The plenary session noted that the scientific work dealing with the problem of blood substitutes proceeds on the whole in a satisfactory manner. However, work on the problem relative to the mass introduction of blood substitutes into production and into general practice has not advanced sufficiently. One of the most important tasks is the speedy initiation of the production of new preparations on a plant scale once they have been approved. Further research aiming at the improvement of the quality of blood substitute solutions and at the creation of new solutions of this type is necessary. It is also necessary to continue detailed investigations on the nature of proteins and on their antigenic and anaphylactogenic properties and to expand work on ways of producing preparations from heterogeneous blood which would be devoid of anaphylactogenic properties to the greatest possible extent and at the same time retain a high therapeutic effectiveness.

Because of the great importance of problems connected with the pathogenesis and therapy of burns, reports in this field are worthy of particular attention. New data on this subject were presented by Prof N. A. Fedorov and S. V. Skurkovich (TsOLIPK). In experiments on dogs these two investigators demonstrated that two toxic components are present in burned tissue. One of these components is similar to thrombin. On intravenous administration, it brings about rapid death. The second component exerts its toxic action after an incubation period of a definite length (3-5 days). The authors of the report isolated specific autoantigens in the organism of burned animals. The isolation of these autoantigens has created favorable conditions for the development of methods whereby a specific noninfectious immunotherapy of burns can be carried out. By the active immunization with the blood of burned animals and also by applying heteroimmunization, the authors obtained an antiburn serum, the therapeutic effectiveness of which has been confirmed in experimental work and at the clinic. On the basis of the results reported, the authors of the report arrived at the conclusion that the prospects for applying immunotherapy of burns are good and that this method of treatment will be very effective.

STAT

Because experimental investigations yielded positive results, the Surgical Clinic of TsOLIPK (head Prof D. M. Grozdov) and the Chair of Clinical and Military Field Surgery (chief Prof A. S. Rovnov) undertook the investigation of the immunotherapy of burns under clinical conditions. L. N. Pushkar' (TsOLIPK) presented convincing clinical data which testified to the effectiveness of isogenic blood and isogenic serum of convalescents in the comprehensive therapy of burns. Immunotherapy carried out on burned patients in the acute stage of toxemia yielded positive results. Of great interest were the data presented by the author of the report which indicated that heterogenic serum is effective in the therapy of burns.

M. P. Khokhlova (TsOLIPK) presented convincing data obtained in the pathological investigation of animals in different stages of toxemia when various methods of hemotherapy had been applied. A comparative study of different methods of hemotherapy (with the use of isogenic serum, plasma, blood, exchange transfusions, dextran, etc) enabled Khokhlova to arrive at the important conclusion that the serum and blood of animals in the convalescent stage exert a beneficial effect.

The data which had been obtained in comprehensive investigations at TsOLIPK dealing with burns indicate that the immunological approach to problems of the pathogenesis and therapy of burns is very promising.

In reports made by D. V. Suzdaleva, V. Ya. Kozlova, Prof G. V. Derviza, and V. N. Smidovich (TsOLIPK), data were presented that had been obtained in investigations of the fractional composition and lability of the protein groups of the blood and also data on disturbances of the oxidation processes in cases of burns.

The present status of problems pertaining to the clinical aspects and therapy of burns was outlined in a report by Prof N. N. Priorov, Active Member of the Academy of Medical Sciences USSR.

As far as the investigation of the pathogenesis and therapy of shock resulting from burns is concerned, Prof I. I. Petrov, Corresponding Member of the Academy of Medical Sciences USSR, presented interesting data which confirm the predominant role of the neurogenic factor in the development of the complex of symptoms accompanying shock due to burns. The author of the report is of the opinion that the therapy of a shock due to burns must proceed along the following lines:

The sensations of pain must be eliminated and the disturbed interrelationship between the processes of excitation and inhibition in the central nervous system must be brought back to normal; hypoxemia must be stopped; disturbances of metabolism must be remedied; the increase in the concentration of the blood must be combated; the development of an infection must be prevented.

Prof T. A. Malivkin and V. Ya. Vasil'kovskan proposed a clinical classification of types of shock produced by burns which would reflect the state of reactive capacity of the organism. Their classification comprises erectile shock, subcompensated shock, and decompensated shock.

I. A. Kotov pointed out the role of the vagosympathetic reflex block in the prophylaxis and therapy of shock resulting from burns.

STAT

The significance of the nervous factor in the pathogenesis and therapy of burns was emphasized in a report by G. D. Vilyavin (Institute of Surgery Imeni A. V. Vishnevskiy, Academy of Medical Sciences USSR). In the system of comprehensive therapy of shock resulting from burns, this author successfully applied a bilateral lumbar or sheath novocain block combined with blood transfusions. The complex of therapeutic measures developed at this institute made it possible to lower sharply the mortality due to shock resulting from burns. The total lethality in a group consisting of 70 patients comprised 2.7%, while in cases of burns of the second degree healing without suppuration took place in 93% of the cases. Vilyavin recommended that plastic surgery by means of skin flaps be applied at an early stage, stating that this type of surgery prevents the development of complications due to infection and contractures and significantly shortens the time of treatment.

In reports by Prof. N. N. Priorov, Active Member of the Academy of Medical Sciences USSR, Prof. E. Yeolyan, Corresponding Member of the Academy of Medical Sciences USSR, Prof. Fishman, Prof. G. S. Ivakhnenko, and others, the occurrence in connection with burns of diverse disturbances of the vascular system, of the organs of hemopoiesis, of metabolism, and of the kidneys was demonstrated. It has been pointed out that one of the causes of inadequate success in the therapy of acute burns is the insufficiently effective use of hemotherapy.

A report by Prof. D. M. Gvozdev (TsOLIPK) dealt with the important problem of establishing differentiated indications and contraindications for blood transfusion, the transfusion of blood substitutes, and the transfusion of antishock liquids depending on the stage of the pathological process due to burns, the seriousness of the condition of the patient, and the composition and directed action of the transfusion agent which is being applied. The author of the report recommends that in the stage of shock one should use antishock solutions in addition to the novocain block and subsequently drop-by-drop transfusion of isoprotein and heteroprotein liquids (i.e., of plasma, LSB, or BK-3).

On the basis of an experimental investigation of the comparative therapeutic effectiveness of blood transfusion, the transfusion of plasma, and the transfusion of serum in shock resulting from burns, F. I. Kovshikov (Leningrad) developed an effective therapeutic method comprising local novocain anesthesia during the first hours of shock, intravenous injection of bromides, and transfusion of preserved blood together with ascorbic acid and vitamin B₁.

Noteworthy was a report by Prof. G. S. Ivakhnenko (Rostov-on-Don) dealing with the therapy of burns with Ye. A. Kon'kov's preparations, i.e., emulsions of honey and fish oil. Emulsions of this type can be easily combined with many therapeutic agents without changing the activity of these agents. Thus, they can be combined with ichthyol, tar, streptocide, penicillin, etc. The rapid healing under the action of these emulsions of wounds due to burns was noted. Bandages saturated with an ointment made of such an emulsion contribute to the rapid detachment of necrotic sections and expedite prolific granulation of surface of the burns.

V. I. Baydak (L'vov) showed in animal experiments that under normal conditions the skin has the capacity to resorb radioactive substance and that the concentration of these substances in the blood increases in the measure in which they penetrate through the skin. The author of the report pointed out that the resorption by a burned surface proceeds several times more rapidly than under normal conditions from normal skin.

STAT

V. P. Koshevaya (TsOLIPK) reported on interesting clinical observations which indicate the effectiveness of using fibrin films in burns.

T. V. Golovin (Leningrad) told about a modification of the method of applying fibrin films in burns by means of which the harmful effect of a tight bandage on the process of regeneration is avoided.

An interesting communication on the treatment of heat burns by the local application of biomyacin and intra-arterial introduction of novocain was made by A. A. Shvets.

P. Ya Sokolov and E. A. Yudovich (Tashkent) reported on a method of treating radiation burns with a new antishock liquid which has the capacity to render harmless the products of protein decomposition and expedites the elimination of these products from the body.

A report by Prof R. O. Yeolyan and S. E. Oganesyan on the comparative evaluation of methods for the therapy of burns was received with great interest. These authors regard as the most effective method of treating burns the careful primary treatment of the burned surface followed by spraying of this surface with a mixture consisting of penicillin and other antibiotics combined with sulfanilamide drugs. The therapy of burned patients is carried out by the open method and heating of the burned surface with electric lamps is applied. During the treatment, transfusions of natural and dried plasma are widely used in addition to the novocain block, appropriate nutrition, and administration of vitamins.

K. F. Dogayeva and S. I. Itkin (Moscow) told about the significance of disturbances of the permeability of capillaries and of hemopoiesis in the pathogenesis of the condition which follows burns. I. V. Il'inskaya (Leningrad) and A. G. Tereshchenko (Rostov-on-Don) discussed the blood formation in the bone marrow in conditions following burns.

On the basis of a discussion of the reports which had been presented, the plenary session arrived at the conclusion that burns should be treated by a many-sided combination of measures adapted to the individual condition of every patient and carried out with consideration for all aspects of the complex pathogenesis of the condition produced by burns.

In a resolution which had been passed, the plenary session emphasized the necessity of expanding investigations dealing with the pathogenesis and therapy of burns.

Progress in the field of atomic energy and in its applications in industry and various fields of science and practical endeavor have set new problems before contemporary medicine. In reports that had been presented at the plenary session, the principal aspects of the therapy of radiation sickness were outlined and the mechanism of the action of radiation on living organisms was partly elucidated.

In a program report read by Prof A. A. Bagdasarov, Corresponding Member of the Academy of Medical Sciences USSR, an analysis of the mechanism of the action of radiation on the body was given and the principal directions along which the therapy of acute and chronic forms of radiation sickness must proceed were discussed. Prof Bagdasarov indicated the significance of comprehensive therapy directed in the acute stages towards restoration of hemopoiesis, of the normal activity of the nervous system, and of the normal functioning of

STAT

the cardiovascular system and also aimed at elimination of the defects of metabolism. The comprehensive therapy of chronic forms of radiation sickness consists in the administration of agents which tend to strengthen the organism, transfusion of blood and blood components, and in addition to that transfusion of leukocytic mass, cationite blood, and various hemostimulants. By using in the chronic forms of radiation sickness the new transfusion agent, i.e., leukocytic mass, Bagdasarov succeeded in obtaining beneficial results in the majority of patients. In a number of cases, the restoration of blood formation functions proceeded very effectively.

A review of the contemporary status of knowledge of the clinical aspects of acute radiation sickness and of the therapy of this sickness was given in a report by Prof. N. N. Kurchakov, Corresponding Member of the Academy of Medical Sciences USSR. In papers by A. P. Belousov and his collaborators (L. L. Shepelovich, M. G. Shitikov, and L. G. Rogachev,) the results of investigations dealing with the destruction of blood and disturbances of iron metabolism in radiation sickness were reported. Methods of comprehensive therapy of the acute form of experimental radiation sickness were also discussed. The authors of the report succeeded in bringing about the survival of a great number of animals which had been subjected to the action of lethal doses of radiation. In a report by Prof. P. N. Kiselev (Leningrad) interesting deductions were made in regard to the therapy of autoinfections in radiation sickness. Streptomycin proved to be the most effective agent preventing autoinfection.

The plenary session pointed out the great significance of blood substitutes in the comprehensive therapy of radiation sickness. Of special significance is the development of therapeutic and prophylactic procedures to be applied during the period which immediately follows irradiation.

On the basis of the reports which have been presented at the meeting, one may conclude that the preliminary results obtained in the investigation of the pathogenesis of radiation sickness enable us to carry out pathogenetic therapy of this condition in addition to purely symptomatic therapy. The plenary session concluded that a further extended study of the pathogenesis and therapy of radiation sickness is necessary.

The reports on problems connected with the use of blood substitutes and dealing with the pathogenesis and therapy of burns and of radiation sickness, together with the discussion which followed, will undoubtedly contribute to further advances in the theory and practice of Soviet medicine.

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